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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,646	04/27/2001	Bingwei V. Yang	PC 10839A	1585

23913 7590 03/31/2004

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EXAMINER	
SEAMAN, D MARGARET M	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 03/31/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,646	YANG, BINGWEI V.	
	Examiner	Art Unit	
	D. Margaret Seaman	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application was filed 27 April 2001 and claims benefit of Provisional Application 60/200834, filed 1 May 2000. Claims 1-11 are before the Examiner.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. The rejection of claims 1, 3-5, 7 and 9-11 under 35 U.S.C. 102(b) as being anticipated by Venet (US Patent #5,968,952), as stated in paper dated 9/26/2003, is upheld. Venet teaches example 83 on column 33 that is encompassed by the instant claims. Venet's equivalent to Z is benzodioxol. This is a heterocycle which is aromatic, 9-membered, and substituted with 1-4 R3 groups wherein R3 is hydrogen. Claims limited to wherein Z is pyridine or thiophene would be free of prior art.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2, 6 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claim 1 is ambiguous due to the claim (twice) having the phrase "except H but including any optional fused rings referred to above". It is suggested that the phrase be shortened to "except H".

Specifically, claims 2 and 6 are ambiguous due to the claims having (on the second line of claim 2) "Z is a pyridine or thiophene group, including pyridine or thiophene groups substituted with...". This phrase should be rewritten to state "Z is pyridine or thiophene optionally substituted with 1-4 R^3 substituents".

Specifically, claim 8 is ambiguous due to the claim being drawn to a compound but having the word "and" on line 11 of the claim. This leads to the claim being a composition. It is suggested that the claim be rewritten to have "or" in the place of "and".

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 10-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not adequately describe the nexus between the inhibition of the Ras farnesylation receptor and a useful treatment of abnormal cell growth and the treatment of all cancers. Modulation of a receptor involves antagonism, inhibition, agonism and others. These modulations are sometimes opposite reactions to the same receptor. It is not seen where the instant specification adequately describes the nexus between the inhibition of the Ras farnesylation receptor and a useful treatment of a cancer.

3. Claims 10-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working

examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims,
2) The nature of the invention,
3) The state of the prior art,
4) The level of one of ordinary skill,
5) The level of predictability in the art,
6) The amount of direction provided by the inventor,
7) The existence of working examples,
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The nature of the invention is the method of treating abnormal cell growth (cancer) that is treatable by the inhibition of the Ras farnesylation receptor.

The state of the prior art: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable

an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects of all diseases, whether or not the inhibition of the Ras farnesylation receptors would make a difference in the disease. Hence, in the absence of a showing of a nexus between any and all known abnormal cell growth (cancer) and the inhibition of the Ras farnesylation receptors, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of inhibition of the Ras farnesylation receptors.

The presence or absence of working examples: The specification states that the compounds of formulas 1 and 2 were assayed for their ability to inhibit the activity of human farnesyl transferase in vitro and were found to have IC50 values of about less than or equal to 500nM. However, no specific activities have been given nor have the specific compounds tested been identified.

The amount of direction or guidance present: The guidance present in the specification is that of the compounds that were tested work to inhibit farnesyl transferase activity. The specification does not seem to enable a correlation between the inhibition of the Ras farnesylation receptors and the treatment of any and all cancers by inhibiting abnormal cell growth.

The breadth of the claims: The claims are drawn to the treatment of any and all cancers by inhibiting abnormal cell growth by inhibition of the Ras farnesylation receptor with the compounds of claim 1.

The quantity of experimentation needed: The quantity of experimentation needed is undue. One skilled in the art would need to determine what cancers out of all known cancers would be receptive to the inhibition of abnormal cell growth by the inhibition of the Ras farnesylation receptors and then would further need to determine which of the claimed compounds would provide treatment of the cancer.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claim 1 for the treatment of any cancer by inhibiting abnormal cell growth. As a result necessitating one of ordinary skill to perform an exhaustive search for which diseases can be treated by which compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its

successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds of the instant claims, with no assurance of success.

This rejection can be overcome by deleting the claims. Claim 11 is included in this rejection because the pharmaceutical composition is for use in the treatment of abnormal cell growth. A claim limited to the pharmaceutical composition of a compound of claim 1 and an acceptable pharmaceutical carrier would be in better condition for allowance.

4. Claims 1, 3-5, 7 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the scope of enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Z is enabled by the instant specification to the extent that Z is optionally substituted pyridine or thiophene. However, all heterocyclic groups are not enabled.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims,
2) The nature of the invention,
3) The state of the prior art,
4) The level of one of ordinary skill,
5) The level of predictability in the art,
6) The amount of direction provided by the inventor,
7) The existence of working examples,
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The nature of the invention is the method of treating abnormal cell growth (cancer) that is treatable by the inhibition of the Ras farnesylation receptor using a compound of formulas 1 or 2 wherein Z is all heterocycles of 4-10 members.

The state of the prior art: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute

predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects of all diseases, whether or not the inhibition of the Ras farnesylation receptors would make a difference in the disease. Further, it would be highly unpredictable if the specification teaches and tests only pyridine and thiophene for Z and any and all heterocycles for Z are claimed. Hence, in the absence of a showing of a nexus between any and all known heterocycles and specifically pyridine and thiophene for the treatment of abnormal cell growth (cancer) and the inhibition of the Ras farnesylation receptors, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 (Z=pyridine or thiophene verses Z= any and all heterocycles) due to the unpredictability of the role of inhibition of the Ras farnesylation receptors.

The presence or absence of working examples: The specification states that the compounds of formulas 1 and 2 were assayed for their ability to inhibit the activity of

human farnesyl transferase in vitro and were found to have IC50 values of about less than or equal to 500nM. However, no specific activities have been given nor have the specific compounds tested been identified. The compounds of formulas ! and 2 generically include Z being heterocycle but the only examples in the specification have Z being pyridine or thiophene.

The amount of direction or guidance present: The guidance present in the specification is that of the compounds that were tested work to inhibit farnesyl transferase activity. The only compounds made have Z being pyridine or thiophene. This leads the ordinary artisan to believe that only pyridine and thiophene can work as Z. The specification does not seem to enable a correlation between the inhibition of the Ras farnesylation receptors and the treatment of any and all cancers by inhibiting abnormal cell growth.

The breadth of the claims: The claims are drawn to the treatment of any and all cancers by inhibiting abnormal cell growth by inhibition of the Ras farnesylation receptor with the compounds of claim 1.

The quantity of experimentation needed: The quantity of experimentation needed is undue. One skilled in the art would need to determine what heterocycles work when the only examples are wherein Z is pyridine and thiophene out of all known heterocycles and then to be receptive to the inhibition of abnormal cell growth by the inhibition of the Ras farnesylation receptors and then would further need to determine which of the claimed compounds would provide treatment of the cancer.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claim 1 for the use of compounds of formula 1 wherein Z is other than pyridine or thiophene for the treatment of any cancer by inhibiting abnormal cell growth. As a result necessitating one of ordinary skill to perform an exhaustive search for which other heterocycles can be used to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to determine which heterocycles for Z other than pyridine or thiophene would work in the instant claims, with no assurance of success.

This rejection can be overcome by amending Z to be pyridine or thiophene.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Margaret Seaman whose telephone number is 571-272-0694. The examiner can normally be reached on 630am-4pm, First Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. Margaret Seaman
Primary Examiner
Art Unit 1625

dms